

SENT BY:

10-4-94; 9:38AM;

U.S. LAB-FOLEY & LARDNER, DC B# 6/14
LONB LAB# 6/7



40399/119/NHND

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re patent application of

Matsui, et al.

Serial No. 07/915,884

Filed: July 20, 1992

Group Art Unit: 1807

Examiner: Marschel, A.

For: TYPE α PLATELET-DERIVED GROWTH
FACTOR RECEPTOR GENE

DECLARATION UNDER 37 CFR 51.132

OCT 17 1994

RECORDED

The Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

Sir:

I, Donald P. Bottaro, being duly warned, hereby declare and
say:

1. I hold the degree of Ph.D. and am currently employed at the National Cancer Institute, the National Institute of Health. I have worked in the field of growth factor/receptor interaction since 1988. My curriculum vitae is attached as Exhibit A.

2. I have reviewed U.S. patent application Serial No. 07/915,884, entitled "Type α Platelet-Derived Growth Factor Receptor Gene" ("the application"). In particular, I have considered the data presented in Figure 11 and the description of these data on page 52 of the specification.

3. Figure 11 is a saturation curve depicting the saturable binding of Platelet Derived Growth Factor ("PDGF") AB or PDGF BB with PDGF α or PDGF β receptors on human D32 cells. The large graph shows that as more PDGF is added, binding continues to increase until a plateau is reached. The inset in this figure

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Serial No. 07/915,884

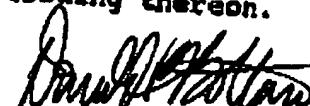
shows the same data, replotted in the standard Scatchard format.

4. Based upon my experience in preparing and using the type of data presented in Figure 11, I would interpret these data as showing that a platelet derived growth factor receptor protein binds the AB and BB forms of PDGF with equivalent affinity. Binding affinity can be estimated from a Scatchard graph. The slopes of the lines drawn through the various points indicate a high binding affinity relative to other known growth factors. At page 52 of the application, the applicants state that binding affinities expressed in terms of K_d were 0.4 nM and 0.5nM for PDGF α receptor and PDGF β receptor cells, respectively. I believe that these K_d values indicate high binding affinities, relative to other known growth factors.

5. I further declare that all statements made herein or my own knowledge are true, and that all statements made on information and belief are believed to be true; and further that these statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements and the like so made may jeopardize the validity of this declaration, the subject application and any patent issuing thereon.

Date

10/4/94


Donald P. Bottaro, Ph.D.

October 1994

CURRICULUM VITAE

Name: Donald Paul BOTTARO

Date and Place of Birth: August 22, 1956; Bridgeport, CT

Citizenship: United States

Marital Status: Married

Education:

1978 B.A. (Biology), The University of Chicago, Chicago, IL
1986 Ph.D. (Cell and Molecular Biology), Boston University,
 Boston, MA

Brief Chronology of Employment:

1985 - 1987 Research Fellow, Elliott P. Joslin Research Laboratory,
 Joslin Diabetes Center, Department of Medicine,
 Harvard Medical School, Boston, MA
1987 - 1990 Intramural Research Training Fellow,
 Laboratory of Cellular and Molecular Biology,
 National Cancer Institute, Bethesda, MD
1990 - Senior Staff Fellow,
 Laboratory of Cellular and Molecular Biology,
 National Cancer Institute, Bethesda, MD

Honors and Other Special Scientific Recognition:

1980 - 1984 Teaching Fellowship, Graduate School of Arts and
 Sciences, Boston University
1983 Dean's Award, Graduate School of Arts and Sciences,
 Boston University
1985 Graduate Scholarship, Graduate School of Arts and
 Sciences, Boston University
1986 Young Investigator of the Year, American
 Microcirculatory Society
1987 National Research Service Award, U. S. Public Health
 Service (Declined in favor of IRTA Fellowship)
1989 Foundation for Advanced Education in the Sciences
 Travel Award, 7th International Conference on Cyclic
 Nucleotides, Calcium, and Protein Phosphorylation.
 October 8-13, Kobe, Japan.

Honors and Other Special Scientific Recognition (cont'd):

1993 **Federal Technology Transfer Award, NCI**
1994 **Federal Technology Transfer Award, NCI**

Societies:

American Association for the Advancement of Science
American Society for Cell Biology

Research Interests:

Signal transduction by growth factors and hormones

Patents:

Aaronson S.A., Ishibashi T., Bottaro D.P., and Miki T. U.S. Patent Pending
Application No. 7/988,273: Expression Cloning of a Human Phosphatase.

Bottaro, D.P., Rubin, J.S., and Aaronson, S.A. U.S. Patent Pending
Application No. 8/059,030: KGF Receptor-Derived Antagonists of KGF
Binding.

Bottaro D.P., Rubin J.S., Faleitto D.L., Chan A.M-L., Vande Woude G., and
Aaronson S.A. U.S. Patent Pending Application No. 7/642,971: Hepatocyte
Growth Factor Receptor is the *met* Proto-Oncogene.

Chan A.M-L., Rubin J.S., Bottaro D.P., and Aaronson S.A. U.S. Patent
Pending Application No. 7/655,502: A Non-Mitogenic Competitive HGF
Antagonist.

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4. Bottaro, D.P. and King, G.L.: The processing and transport of peptide hormones across endothelial cell barriers. In: *Insulin, Insulin-like Growth Factors, and Their Receptors in the Central Nervous System*. Raizada, M.K. Phillips, M.F. and LeRoith, D. (Eds.), Plenum Publishing Corp., New York, 1987.
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